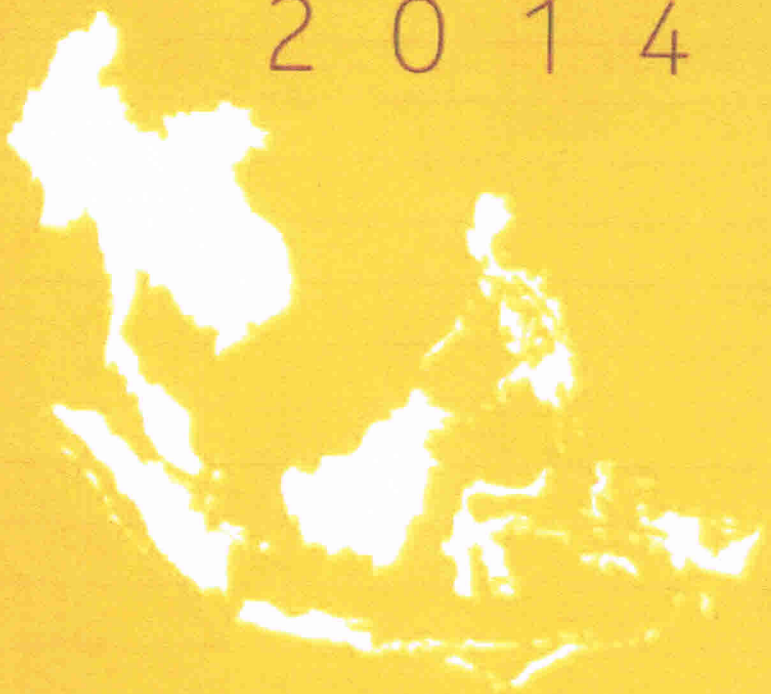
ASEAN ENDODONTIC FORUM 2014



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CONTENTS

The beneficial antioxidant effect of minocycline 0,1% reduced bleeding on gingival inflammation

Dr. Ernie Maduratna Setiawati

ABSTRACT

Background

Minocycline, have been shown to suppress the growth of bacteria plaque. Minocycline was reported to induce cytoprotective effects in gingival epithelium induced Agregatebacter actinomyctemcomitans. The beneficial effects of the minocyclines were shown to be related to a reduction of the inhibition of inducible nitric oxide synthase and interleukin (IL)–1β expression. The rationale of the study is based on our previous studies demonstrating the beneficial antioxidant effect of minocycline 0,1% in vitro.

Purpose

The aim of the present study is to assess the clinical efficacy of minocycline 0,1% oral rinse in managing of gingival inflammation.

Material and method

Patients with bleeding on gingiva will randomly receive minocycline rinses. Thirty adult chronic periodontitis patient divided into two groups . group 1 : comprised fifteen chronic periodontitis involved sites managed by scaling root planing alone. And group II : comprised fifteen chronic periodontitis involved sites treated by the same technique in adjunct with the application of antioxidant mouth rinse minocycline. Clinical examination include bleeding on probing (BOP) with papilla bleeding index.

Result

These findings suggest that minocycline oral rinse 0,1% may actually decrease bleeding on gingiva significantly ($p<0,05$).

Conclusion

We report that minocycline provides inhibitor effect against bleeding on gingiva. Minocycline 0,1% as an antioxidant effect potential as adjunct theurapetic agent to reduce gingival bleeding.

INTRODUCTION

Oxidant and bacterial deposits play an essential role in pathogenesis of gingival inflammation. Gram negative anaerobes were predominantly isolated than gram positive in periodontitis cases.[1,2] The presence of pathogen alone is not sufficient to cause periodontal inflammation. Bacterial pathogen gram negative anaerobes stimulate host cells to release proinflammatory cytokines. This cytokines recruit PMNs to produce proteolytic enzymes such as elastase, collagenases and molecular oxygen by oxidative burst.[3-5] Free radicals highly reactive and diverse species, capable of extracting electrons and thereby oxidizing a variety of biomolecules vital to cell and tissue functions. Periodontal tissue destruction leads to overproduction of lipid peroxides, inflammatory mediator and oxidized proteins. These products further activate macrophages, neutrophils and fibroblast to generate more ROS.[6] The disturbance of this equilibrium between the free radicals and antioxidant is the prerequisite for healthy periodontal tissue, so has led to search for appropriate antibacteri therapy and anti oxidant therapy for prevention and treatment of periodontal inflammation.[7,8]

Minocycline is a semi-synthetic tetracycline with broad-spectrum antibacterial activity in addition to their antimicrobial effect have been shown to anti oxidant effect. In addition to antimicrobial activity, minocycline exerts immunomodulatory effects via suppression of T lymphocytes and PMNs leading to reduction of tissue destruction attributed to active T cells and PMNs. Minocycline delays T cell proliferation associated with IL-2 activity and suppresses T cell production of interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α), which play a role in the epithelial damage. Minocycline in vitro delayed the migration of PMNs and reduced phagocytic activities of the PMNs. It also was reported that incubation of PMNs with minocycline suppressed the tissue damage linked to PMN activity.[8] Bleeding on probing (BOP) is a widely used criterion to diagnose gingival inflammation. BOP useful prognostic indicator in clinical diagnosis for patients in periodontal disease. The purpose of this study was to evaluate the clinical efficacy of a minocycline mouth rinse in reducing bleeding on probing in gingival inflammation.

Method

Thirty patients with gingival inflammation were enrolled for this study. All subjects signed institutional approved informed consent and were clinically diagnosed with chronic periodontitis. All subjects were otherwise healthy individuals as documented in health history. None had any contraindication to use of tetracycline medications (allergy, breast-feeding, pregnancy and age less than 12 years). Using a random numbers computer program, qualified patients were randomly, starting the treatment

with minocycline 0,1% mouth rinses. They were divided into two groups, where group 1 : comprised fifteen chronic periodontitis involved gingival bleeding sites managed by scaling root planing alone. And group II : comprised fifteen chronic periodontitis involved gingival bleeding sites treated by the same technique in adjunct with the application of antioxidant mouth rinse minocycline 0,1%. Clinical examination include bleeding on probing (BOP) with sulcus bleeding index. The rinses were prepared based upon the effective antioxidant dosage of the medications, subjects used 0.1 % aqueous solution of minocycline as mouthrinse. The preparations were of similar consistency without color. The subjects were instructed to begin mouthwashes as randomly assigned. They were instructed to rinse their mouth with tap water prior to the administration of the study rinse and then to rinse with 5ml of the solution for 30 second, two times a day avoiding any food or drink for at least ½ hour after the rinses. Therapy continued for up to 14 days. Examiner A using a standardized periodontal probe (CP11 Hu Friedy, Europe) detected Bleeding on Probing (BOP). The BOP was considered positive if bleeding occurred between 30 seconds after probing and used Sulcus Bleeding Index (SBI).

Sulcus Bleeding Index (SBI)

An early sign of gingival inflammation is bleeding on probing. Muhlemann and Son (1971) described the Sulcus Bleeding Index (SBI). The criteria for scoring are as follows:

Score 0 – health looking papillary and marginal gingiva no bleeding on probing;
Score 1 – healthy looking gingiva, bleeding on probing;
Score 2 – bleeding on probing, change in color, no edema;
Score 3 – bleeding on probing, change in color, slight edema;
Score 4 – bleeding on probing, change in color, obvious edema;
Score 5 – spontaneous bleeding, change in color, marked edema.

Four gingival units are scored systematically for each tooth: the labial and lingual marginal gingival (M units) and the mesial and distal papillary gingival (P units). Scores for these units are added and divided by four. Adding the scores of the undivided teeth and dividing them by the number of teeth can determine the sulcus bleeding index. Statistical analyses were conducted using the T-test for independent samples.

Results and Discussion

Table 1: sulcus bleeding index score at minocycline oral rinse treatment and SRP treatment sites

Treatment	Sample size	Day 0 SBI score	Day 14 SBI score	p value
SRP	15	4,6	0,73	$p < 0,05$
SRP + MINOCYCLINE	15	4,7	0,17	$p < 0,05$

Periodontal diseases are primarily inflammatory in nature, the ability to detect inflammatory lesions in gingival tissues is essential for the diagnosis and monitoring of changes in periodontal status. One of the first clinical signs of progressivity of gingival inflammation is the bleeding on probing. Bleeding occurs because of frequent micro-ulcerations in the epithelium probing that lines the gingival sulcus/periodontal pocket. Bleeding on probing has been used as a key parameter in the evaluation of periodontitis because of its objectivity and ease of clinical access. Analyses of gingival biopsies with an inflammatory cell infiltrate in the gingival tissues are correlated with visual signs of inflammation and bleeding on probing. Bleeding on probing (BOP) is an indicator of tissue inflammatory response to bacterial pathogens. Due to anatomical limitations, the entity and physical state of microbial aggregations located under the gingival margin and their relations to BOP have been hardly investigated till now. The bleeding on probing (BOP) is a widely used clinical sign as indicator of the periodontal condition and disease progression.[9]

Reactive oxygen species (ROS) are physiologically produced by the cellular metabolism. Exogenous sources of ROS are smoking, ultraviolet light, heat, ultrasound, ozone, radiation, bacteria infection, excessive exercise, trauma, and drugs, whereas endogenous sources include products of metabolic pathways and products of immune and connective tissue cells. Antioxidants are substances that can inhibit the action of oxidant species. There is a physiological fine balance between oxidant activities and antioxidant defenses, but when this equilibrium is disrupted to the advantage of ROS, or to increased ROS activity or to want of antioxidant defenses, the result is oxidative stress. An amplified activity of ROS implies a large spectrum of molecular and cellular damage. This results in covalent binding with proteins, which alters their structure and function. Some oxidized proteins are difficult to remove by cells and tend to accumulate with aging and in the presence of chronic diseases such as chronic periodontitis.[7,8]

Minocycline is a semi-synthetic tetracycline with broad-spectrum antibacterial activity in addition to their antimicrobial effect have been shown to anti oxidant effect. Minocycline prevents oxidative protein modifications and damage in disease models associated with inflammatory activation and oxidative stress. Although the drug has been assumed to act by preventing the up-regulation of proinflammatory enzymes, minocycline is direct chemical interaction with reactive oxygen species. The antibiotic did not react with superoxide or •NO radicals, but peroxynitrite. The antioxidant activity of minocycline extended to cellular systems, because it prevented mitochondrial DNA damage and glutathione depletion.[10,11]

Its clinical relevance has been shown that the decrease of mean level of bleeding on probing favor of minocycline starting on 7 day ($p < 0.05$). A study on this topic, demonstrates that the absence of BOP represents a reliable indicator of periodontal stability. Besides, the value of BOP as predictor of future periodontal deterioration seems to significantly increase when associated with periodontal pocket depth. Bleeding on probing (BOP) is a widely used criterion to diagnose gingival inflammation. Many factors can influence bleeding, including medications, systemic diseases, and smoking. In this study showed that significant decrease BOP was seen with minocycline mouthrinse compared to control. These findings suggest possible use of minocycline for prevention of progressivity of periodontitis. The concentration of minocycline rinse in the current study (0.1%). It was based upon the minimum inhibitory concentration of the subgingival bacteria and antioxidant effect as used in a previous study. In high doses, systemic minocyclines may be associated with changes in cutaneous pigmentation and accumulation of derivates may occur in bones and developing teeth. Topical minocyclines for chronic periodontitis also report a lack of major side effects. The topical use of minocycline was based on the assumption that a bacterial etiology accompanies the onset of chronic periodontitis. However, the impact of minocycline upon

cytokine production, cellular degranulation and collagenase activity may represent the mechanisms of action has been documented in periodontal disease.[12] The current study, strongly suggests that topical minocycline may have greater impact upon the tissue damage and healing. Administration of minocycline 0,1% as an adjunct to scaling and polishing resulted in statistically significant improvements in periodontal clinical status, and significant reductions of pocket depth and bleeding on probing. The results of the present study show that minocycline rinses 0,1% are significantly effective for management of gingival inflammation.

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